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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,927	02/20/2004	Ronald A. Fleming	066438-5001US	7276

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EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
10/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/783,927	FLEMING ET AL.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 12-65* is/are pending in the application.

4a) Of the above claim(s) *2-6 and 14-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7,8,12,13 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Applicants' response and amendments to the claims, filed 7/7/2008, are acknowledged and entered. Claims 9-11 have been cancelled by Applicant. Claims 1-8 and 12-65 are pending and under examination. Claims 2-6 and 14-64 remain withdrawn from consideration as being drawn to non-elected inventions/species. Accordingly, claims 1, 7-8, 12-13, and 65 are the subject of this Office Action.

Response to Arguments

Any previous rejections and/or objections to claims 9-11 are withdrawn as being moot in light of Applicant's cancellation of the claims.

Claim Rejections - 35 USC § 112 – 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7-8, 12-13, and 65 are again rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

Regarding the requirement for adequate written description of chemical entities, Applicant's attention is directed to the MPEP §2163. In particular, *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plain for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for

Examination of Patent Applications under the 35 U.S.C. 112.I "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics when coupled with a known or disclosed correlation between function and structure..." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting *Guidelines*, 66 Fed. Reg. at 1106 (emphasis added)). Moreover, although *Eli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. *Univ. of Rochester v. G.D. Searle & Co.*, 249 Supp. 2d 216, 225 (W.D.N.Y. 2003).

In the instant case, the claims recite a genus of compounds of Formula (I) or "prodrug thereof" (*e.g.*, claim 1). There is insufficient written description of the claimed prodrugs of compounds of Formula (I).

Despite the disclosure that "prodrugs" of the claimed compounds of Formula (I) are encompassed by the claims (*e.g.*, claim 1; page 22 of specification), it remains that the specification provides no chemical structures or description of the compounds described as "prodrugs" that may be used within the context of the present invention. It has been held in patent law that a wish or plan for obtaining the invention as claimed does not provide adequate written description of a chemical invention. Rather, a precise definition, such as by structure, formula, chemical name or physical properties or a combination thereof, is required. Please reference, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004). In other words, though Applicants may have a plan for how to identify other agents that may be amenable for use in the present invention (such as the claimed prodrugs), it remains that at the time of the invention, Applicants had not identified such compounds, and, therefore, did not have written description of the full scope of the genus claimed.

Applicant's arguments have been carefully considered but they are not persuasive. Applicants argue that the specification "has clear and specific description of 'prodrugs'". Applicant's description of the claimed prodrugs encompass "...any pharmaceutically acceptable

form (such as an ester, amide, salt of an ester, salt of an amide or a related group) of the compounds described herein that, upon administration to a patient, provides the active compound." and "... compounds that are metabolized, for example, hydrolyzed or oxidized, in the host to form the compound of the present invention. Typical examples of prodrugs include compounds that have biologically labile protecting groups on a functional moiety of the active compound. Prodrugs include compounds that can be oxidized, reduced, aminated, deaminated, hydroxylated, dehydroxylated, hydrolyzed, dehydrolyzed, alkylated, dealkylated, acylated, deacylated, phosphorylated, dephosphorylated to produce the active compound. The compounds of this invention possess antiviral activity against a togavirus and/or coronavirus or are metabolized to a compound that exhibits such activity." (See specification at page 62, first paragraph and page 63, third paragraph). However, contrary to Applicant's assertion that these descriptions of prodrugs "clearly convey claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention at the time the application was filed", the description in the specification of the claimed prodrugs only demonstrates that Applicants knew what prodrugs, in general, were and what they did. However, it remains that there is no structural description of prodrugs of the claimed compounds in the specification. In other words, Applicants have not provided any structures of compounds of Formula I that have the claimed properties, e.g., compounds that are metabolized, for example, hydrolyzed or oxidized, in the host to form the compound of the present invention, but rather leave it up to the skilled artisan to determine what modifications, out of all the modification that might be made to compounds of Formula I, would result in a "prodrug".

Accordingly, the rejection is maintained for the reasons of record and as reiterated above.

Claim Rejections - 35 USC § 103 – New Ground of Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The instant rejection is necessitated by Applicant's amendments to claim 1, which removed the limitation "herpes virus" from the claims.

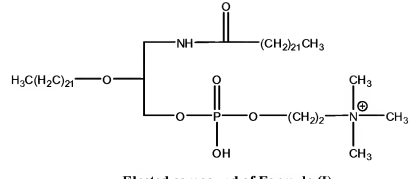
Claims 1, 7-8, 12-13, and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Kucera *et al.*** (USP No. 5,962,437; Issued Oct. 5, 1999) in view of **Holmes *et al.*** (New England Journal of Medicine, 2003, vol. 348, no. 20, pages 1948-1951.

The instant claims (as amended) recite methods of treating a host infected with a togavirus or a coronavirus (elected), comprising administering a compound of Formula (I) as recited in claim 1 wherein,

R_1 is –NHC(O)Y, where Y is C_{22} alkyl;

R_2 is –OX, where X is C_{22} alkyl; and

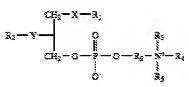
R_3 is phosphocholine.



Elected compound of Formula (I)

Kucera *et al.* teach methods of treating viral infections, and in particular HIV-1, hepatitis B virus, and herpes viruses, comprising administering an infection-combating amount of a

phospholipid or phospholipid derivative (Abstract). In particular, compounds of Formula (I) are disclosed, wherein R_1 is a C_6 to C_{18} alkyl group, X is NHCO, R_2 is C_6 to C_{14} alkyl, Y is O, R_6 is C_2 to C_6 alkyl, and R_3, R_4, and R_5 are methyl or ethyl (col. 2, lines 3-35):



(I)

Compounds of Formula I (Kucera *et al.*)

The compounds of Formula (I) disclosed in Kucera *et al.* are taught to attach to the cell membrane and thus are particularly effective against infections caused by membrane-containing or envelope containing viruses (col. 9, lines 42-45), including herpes viruses as instantly claimed (col. 9, line 59). The administration routes recited in instant claim 65 are taught at column 10, lines 14-21.

The cited reference differs from the instant claims in the length of the alkyl chains at R_1 and R_2 in the compounds of Formula (I). For example, the elected compound of Formula (I) has a C_{22} alkyl chain at R_1 and R_2, whereas the reference limits these substituents to C_6 to C_{18} alkyl and C_6 to C_{14} alkyl, respectively. Kucera also differs from the claims in that the reference does not disclose the treatment of a corona virus (*e.g.*, SARS-CoV).

However, Kucera *et al.* suggest and motivate the treatment of any virus type, especially membrane-containing or envelope containing viruses, wherein they teach that the compounds of Formula (I) disclosed therein attach to the cell membrane and thus are particularly effective against infections **caused by** membrane-containing or envelope containing viruses (col. 9, lines 42-45). Holmes *et al.* is provided as evidence that it was known in the art at the time of the invention that SARS corona virus contains a viral envelope (page 1949, right column and figure on page 1949).

It would have been *prima facie* obvious at the time the invention was made to lengthen the alkyl chain length of the R_1 and R_2 substituents in the compounds of Formula (I) as disclosed in Kucera *et al.* Such extending of alkyl chain lengths would have been obvious to one of ordinary skill in the art because members of a homologous series of chemical compounds would

be expected to possess the same principal characteristics which vary gradual from member to member. See *In re HASS AND SUSIE*, 60 USPQ 548 (C.C.P.A. 1944) and *In re NORRIS*, 84 USPQ 458 (C.C.P.A. 1950). As such, one skilled in the art would have been imbued with at least a reasonable expectation that compounds of Formula (I) as disclosed in Kucera *et al.* having longer chain lengths would also be effective in treating viral infection such as infections **caused by** membrane-containing or envelope containing viruses as suggested and motivated by Kucera *et al.* See *In re NORRIS*, 84 USPQ 458 (C.C.P.A. 1950) wherein the court, citing 31 C.C.P.A. (Patents) 895, 903 and 908; 141 F.2d 122, 127 and 130; and 60 USPQ 544, 548 and 552 ("Hass *et al.*" cases) affirmed that "novel members of a homologous series of chemical compounds must possess some unobvious or unexpected beneficial properties not possessed by a homologous compound disclosed in the prior art." In the instant case, no unobvious or unexpected beneficial properties of the elected compound of Formula (I) have been proffered.

With respect to it the treatment of a coronavirus as recited in the instant claims, it would have been *prima facie* obvious at the time of the invention to treat a corona virus, particularly a SARS corona virus, using the methods of Kucera *et al.* The skilled artisan would have been imbued with at least a reasonable expectation that such treatment of a corona virus would be successful because Kucera *et al.* teach that the methods of treating viral infections disclosed therein are "particularly effective against infections caused by membrane-containing or envelope containing viruses". Thus, it would have been obvious to treat any type of virus infection wherein the virus was known to contain a membrane or envelope using the compounds suggested and motivated by Kucera *et al.* because the inventors therein suggest (and even claim) the treatment of "viral infection", exemplifying the treatment of herpes viruses, with the compounds of Formula (I) disclosed therein, and Holmes *et al.* teach that SARS corona virus contains a viral envelope and is thus reasonably a type of virus intended to be treated using the methods disclosed in Kucera *et al.* As such, one of ordinary skill in the art would have been motivated to treat membrane-containing or envelope containing viruses such as SARS corona virus as suggested and motivated by Kucera *et al.* in view of Holmes *et al.*

Applicant's arguments have been carefully considered but they are not persuasive. Firstly, Applicants argue that independent claim 1, as amended, is patentable over Kucera because Kucera does not teach or suggest the treatment of a togovirus or coronavirus. This

argument is not persuasive because the present rejection, which is necessitated by Applicant's deletion of "herpes virus" from claim 1, is based on a combination of references, not Kucera alone. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Secondly, Applicants argue that Kucera does not teach or suggest applying lipid analogs to explicitly treat coronavirus infections as recited in the instant claims. This is true. However, Kucera does teach and suggest treating viruses, especially membrane-containing or envelope containing viruses, wherein they teach that the compounds of Formula (I) disclosed therein attach to the cell membrane and thus are particularly effective against infections **caused by** membrane-containing or envelope containing viruses (col. 9, lines 42-45). Holmes *et al.* is provided as evidence that it was known in the art at the time of the invention that SARS corona virus contains a viral envelope (page 1949, right column and figure on page 1949). Applicants have presented no evidence for the assertion that "the interactions of envelop-structured viruses with the host cell can occur in many different and unpredictable ways". However, even if this were true, Kucera, in contrast to Applicant's characterization, does provide a working mechanism with regard to the use of lipids in treating virus infections, especially membrane-containing or envelope containing viruses, wherein they teach that compounds of Formula (I) disclosed therein attach to the cell membrane and thus are particularly effective against infections **caused by** membrane-containing or envelope containing viruses (col. 9, lines 42-45).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614